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# LEWISITE AND OTHER ARSENICAL VESICANTS

by

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## I. INTRODUCTION

The arsenical vesicants which we shall consider for the next forty-five minutes all contain arsenic in the trivalent form. Usually two of these valences are taken by chlorine, i.e., the compounds are of the type  $RAsCl_2$ , in which R represents an aliphatic or aromatic substituent group.

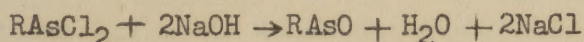
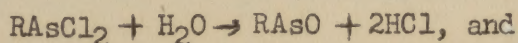
I shall deal primarily with four arsenical vesicants of this type, and what is said about one of them, unless otherwise stated, applies to other compounds of this type. The compound of primary interest is lewisite or M-1 which is dichloro (2-chlorovinyl) arsine. The other three compounds which we shall consider are: dichloroethylarsine (ED), dichloromethylarsine (MD), and dichlorophenylarsine (PDA).

We shall consider some of the important physical and chemical properties of these compounds in a moment, but it seems best at this point, to classify them physiologically. They are introduced here as vesicants, but as is the case with the mustards their action is not limited to this one function. Indeed they surpass the "triple threat" mustards by having even greater versatility and may well be called "quintuple threat" agents.

In addition to their vesicant powers the dichloroarsines are pulmonary irritants, lachrimators, sternutators, and finally systemic poisons. M-1, ED, and similar compounds thus combine in one agent all of the harmful properties one might expect to find only in a number of chemically diverse compounds. We have then a series of war gases of great potential value, of whose characteristics we should be aware, and whose effects we should be prepared to avoid, recognize and combat.

## II. CHEMICAL AND PHYSICAL PROPERTIES

One of the most distinctive properties of the dichloroarsines is their reaction with water or alkalies. The type reactions are:



That is, the two chlorine groups are removed and the compound is converted to the corresponding arsine oxide. This is important for

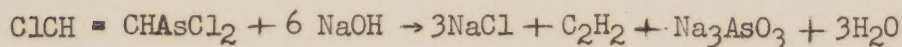


two reasons:

- a. The oxide is ordinarily of lesser volatility than the dichloroarsine and the danger from vapor concentrations is correspondingly decreased. Wet terrain will decrease the danger from vapor of these compounds, and wet clothing or wet blankets over the openings in gas shelters may be expected to afford a measure of protection against the vapors.
- b. The oxides are in most cases less toxic than the parent dichloroarsine.

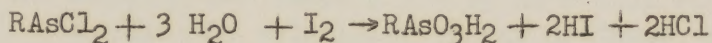
Lewisite is an exception in two ways to the above:

- a. The oxide of lewisite is a very toxic compound and is a powerful vesicant. Consequently, when lewisite is hydrolysed to the oxide, this compound will remain on the ground and other surfaces for a long time and be dangerous to those who come in contact with it.
- b. While lewisite is converted to the oxide in the presence of water or weak alkalis, the reaction with strong alkalis goes beyond hydrolysis, the chlorovinyl group is attacked, and the lewisite is converted to an arsenite. Thus,



The compound is in this way effectively destroyed.

A second important chemical property of the dichloroarsines is their capacity for being oxidized from the trivalent to a less toxic pentavalent form. Thus the reaction with iodine may be symbolized as,



The compounds may be similarly oxidized by hypochlorite (bleach paste), bromine water, or peroxide.

Finally of interest to us here is the fact that these compounds while insoluble in water are very soluble in common organic solvents such as alcohol, carbon tetrachloride, gasoline, and kerosene.

The above chemical properties are the basis for the commonly used methods for neutralizing or decontaminating the dichloroarsines. These are:

1. Conversion of the compound to a less toxic form



by oxidation with peroxide or bleach paste.

2. Hydrolysis (or, in the case of M-1, actual destruction) with alkali solutions, thus converting the compound to a less volatile and somewhat less toxic form.
3. Removal by washing with solvents.

Concerning the physical properties of the dichloroarsines we need to know several facts if we are to recognize these compounds and predict their behavior. They are all mobile liquids having a density 1.8 - 1.9 times that of water. In the pure state they are colorless, but plant run products, or products which have aged are apt to be dark in color, e.g., M-1 to be dark brown, ED to be yellow.

The only one of these compounds having a truly distinctive odor is M-1 which everyone agrees smells exactly like geraniums. More distinctive is the biting stinging sensation which all of them produce in the nose. This occurs at very low concentrations, indeed even with M-1 the nose is irritated before the odor of geraniums is perceived.

The other physical properties of these compounds of interest to us are the melting point, the vapor pressure or volatility at temperatures apt to occur during gassing attacks, and the density of the vapors. The available data are collected in Table I. (See end of lecture.)

As aids in interpreting the data of Table I several facts are of interest:

1. Milligrams per liter of air may be taken as numerically equivalent to ounces per thousand cubic feet.
2. Raising the temperature by 10°C will roughly double the volatility of any of these compounds.
3. Experts estimate that 1/10 - 1/20 of the full volatility of a compound will probably be achieved in the field.

From these facts we can make several important predictions concerning these compounds. Unlike mustard (HS) they will be liquids at most temperatures apt to be encountered. Their vapors are heavy and may be expected to accumulate in low places. PDA and M-1 will be persistent agents while ED and MD will be relatively non-persistent. We must not overlook the fact that non-volatile oxides of any of these compounds may be present for long times after gassing attacks. The danger from M-1 oxide is particularly to be recognized. For a further appreciation of the significance of the



volatility of the several compounds we must consider this feature in relation to lethal concentrations.

### III. TOXICITY

All of the figures which predict the amounts of arsenicals which must be inhaled to cause death are based on animal experiments involving a number of species. For practical purposes we may assume that a law is true which states that concentration multiplied by time of exposure is a constant. Lethal concentrations of these compounds for a ten minute exposure are given in the last column of Table I.

We see that for MD this concentration is roughly one half milligram per liter, and for the remaining compounds three tenths of a milligram, although the concentration of lewisite required is variously given as some place between 0.12 and 0.3 mg. per liter.

Now, you can see that in the case of MD, if there were saturated vapor the concentration would be about 150 times that necessary for a ten minute exposure. For ED it would be roughly 70 or 75 times, for M-1 some 12 to 15 times, and for PDA it would be around 1.3 times that necessary for a 10 minute exposure. Actually in the field there may be only one-tenth to one-twentieth of those saturation concentrations.

These compounds would furnish enough vapor, even if there was only one-tenth to one-twentieth saturation, to make them very aggressive and very dangerous. Prentiss states that a concentration of .3 of a milligram per liter of M-1 vapor will blister a man after a short exposure, so we can see that M-1 is sufficiently aggressive to cause vapor blisters.

In addition Table I gives some data concerning the minimum detectable and intolerable concentrations of these agents. Roughly we can say that one thousandth of a milligram of any of these compounds per liter will be detectable because of its irritating effect. In the case of M-1 at a slightly higher concentration the odor will be detectable. Intolerable concentrations are somewhat higher. One cannot in most cases stand more than one one-hundredth of a milligram per liter of these compounds for more than a minute.

Here, then, is a distinction between these compounds and mustard: The arsenicals give you warning. One-tenth to one-thirtieth of the lethal concentration for a ten minute exposure is intolerable for a minute, so if you have a gas mask you are apt to get it on before you breathe a lethal dose.

In addition to getting a lethal dose by breathing the vapor, however, it is also possible to get a lethal dose of any of these arsenicals by absorption of the compounds through the skin. It has been



estimated by Vedder that 1.4 cc. of liquid lewisite on the skin of a man who received no further attention would be lethal. There are no reliable estimates of the extent of exposure to vapor which would be necessary or the amount of liquid of the other agents which would be necessary, but I think we may assume for purposes of safety that a dose of any of them of the order of the lewisite dose I have just given you would probably be fatal. This is the basis of the often emphasized advantages of arsenical vesicants, as systemic poisoning gases. Such amounts of liquids are most apt to get on the skin in plant or laboratory accidents or in the case of personnel close to chill bursts or spraying attacks with airplanes.

#### IV. TYPES OF CASUALTIES

First, I shall consider briefly eye casualties, not in any detail because they will in all probability be taken up by Dr. Hughes tomorrow morning, but such casualties are so important with respect at least to lewisite that they cannot be overemphasized. Liquid M-1 in the eye cannot fail to produce a very serious casualty. The victim experiences immediate pain as if from a powerful caustic in the eye. Clinical signs develop almost at once. At the end of fifteen minutes there is an acute inflammatory condition of the conjunctiva and pronounced engorgement of the blood vessels. Edema of the lids, intraocular pain, and photophobia, follow rapidly. Within three or four hours there is intense edema of the lids. The eyelids are closed and adhere at their margins. Separation of the lids releases a purulent fluid, and there are sub-mucous hemorrhages, extensive ulceration of the conjunctiva, and a hazy cornea. The condition three or four hours after liquid M-1 is splashed into the eye is more distressing than that produced by liquid mustard in twenty-four hours.

We have then two characteristics of these compounds: First, rapidity of action, and second, the intense pain developed in any exposed part, both of which combine to produce an immediate casualty. M-1 vapor causes intense lacrimation and can produce profound damage to the eye. But I shall leave this subject to be dealt with more fully tomorrow morning.

Liquid M-1 on the skin is followed by a stinging sensation which persists, and which may be well nigh intolerable if any considerable area is involved. Absorption is very rapid. Those of you who had mustard applied to your arms may have seen that the liquid was there a considerable length of time. Had it been lewisite, by the time the rod was removed you would have seen little, if any, liquid on the surface of the skin. Erythema which precedes vesication occurs within fifteen to twenty minutes after the lewisite has been put on. Vesication is usually developed within about twelve hours. At this time a clear distinction can be drawn between the blisters which are caused by M-1 or other arsenicals and those which are caused by mustard.



M-1 burns have rather steep sides to the blister, and there is a very limited surrounding area of erythema. As contrasted with this, the blister of mustard has sloping sides and an intense red area of erythema surrounds it. The M-1 blister is filled with an opaque or opalescent fluid, rich in leukocytes and containing arsenic, whereas the mustard blister fluid is clear and contains no trace of the HS.

This slide shows the hand of a man who accidentally touched a testing rod wet with M-1, and you can see two well marked blisters on the fingers. You will notice that there is practically no surrounding area of erythema.

Burns from the vapor of M-1 may come from the vapor itself in the atmosphere, or more commonly perhaps from the vapor which emanates from splashes of liquid M-1 which get on the clothes. As mentioned before, wet clothing will offer a slight amount of protection against vapor or very small droplets, but certainly in itself should not be depended upon in the case of large droplets. Large drops of M-1 on dry clothing can cause serious burns. When in low concentrations, the vapor may cause no more than erythema, but high concentrations cause widespread erythema with small, shallow, turbid blisters which may coalesce.

This slide shows a burn on the buttocks of a man who sat on a rag which had one drop of lewisite on it. He notices a burning or stinging sensation in about 20 minutes. He had a shower 20 minutes later, and  $1\frac{1}{2}$  hours later peroxide was applied to the burned area. Later butesin picrate ointment was used which was probably unwise. This picture was taken 24 hours after the exposure. You will notice this large blister and a number of small ones here which show some tendency to coalesce with the large one. The next slide was taken four days later. The burned area has been debrided and a sulfadiazine spray employed. This slide is intended primarily to show the pigmentation that has occurred, particularly around the margin here, but you can still see the necrotic burned area in the center.

Next we shall consider casualties that involve the respiratory tract. Exposure to M-1 vapor even in low concentrations will produce irritation of the nasopharynx with symptoms of coryza, salivation, and laryngeal irritation. These are followed by a generalized bronchitis and in severe cases bronchial pneumonia occurs.

In laboratory dogs there is, following exposure, labored respiration, and the nostrils are clogged with a thick membrane. Coughing is frequent and accompanied by the ejection of frothy mucus which has probably been swallowed. Coarse rales are general over the chest indicating an intense bronchitis. Later there is violent sneezing and nasal discharge. There is a slight drop in temperature which returns to normal in 24 hours, and has no diagnostic value with respect to the severity of the casualty.



In man if sufficient quantities of arsenic are absorbed, there are symptoms of arsenical poisoning evidenced by dryness and soreness of the throat, diarrhea and restlessness, and later the nervous system and liver may show some involvement.

The first of the next two slides is a section of a lung, following gassing with MD. You will see in this slide the engorgement of the capillaries, which are well defined. You will also see the protein containing edema fluid which has stained with eosin in the alveoli, and the beginning of the sloughing off of the broncheolar epithelium.

The next slide shows a pneumonia of one lung evidenced by these yellow abscesses.

## V. PROPHYLAXIS AND TREATMENT

Prophylaxis in the case of skin burns as with the other agents must be instituted at once, within a minute if possible. I shall assume that it is possible. Contaminated clothing should be removed immediately with every precaution to prevent the further contamination of personnel. However, prophylactic treatment should be instituted even while this removal of clothing is going on. The contaminated area should first be dried with an absorbent material, if liquid is present, subject to the same limitations Dr. McLean expressed, and the area should then be swabbed repeatedly with 8 per cent hydrogen peroxide, which can be made up from Merck's 30 per cent superoxol. If there is no 30 per cent available, 3 per cent U.S.P. hydrogen peroxide available in any drug store will be the next best. Fresh swabs should be used for each application and destroyed as soon as possible. Swabs should be moist but not dripping.

If there is no peroxide available then a solution of 10 per cent sodium hydroxide in a 30 per cent solution of glycerin in water or 5 per cent aqueous NaOH is next best. This should be used like the peroxide, care being taken to avoid spreading the contamination on the skin. After swabbing with the alkalis, the skin should be washed with 70 per cent alcohol, and following this the skin should be washed with soap and water.

If none of those materials are available, then better than nothing is repeated sponging with organic solvents, such as kerosene, gasoline, carbon tetrachloride or alcohol, to wash the material away, and these should also be followed by washing with soap and water. In this case every care should be taken to keep from washing the compounds over the skin and spreading the arsenical. Protective ointment, which affords protection before contamination should not be used after there has been a development of erythema.

Following the above immediate treatments, relief of the itching



may be accomplished by the use of simple dressings and the use of antipruritic ointment No. 88, which you will find in these Technical Manuals which you have been given.

Severe burns with liquid M-1 may require complete excision of the burned area. This should only be done where the extent of the burn is great and is such as to indicate that perhaps there will be systemic poisoning. It should be carried down to the subcutaneous tissues and the wound should be left open to heal by second intention. In any case, blisters should be drained to prevent absorption of the contained arsenic. It might be well where the burns are extensive to institute such measures as are available for combatting arsenical poisoning, including adequate fluid intake, intravenous glucose, high carbohydrate diet, and vitamin intake.

The remaining measures which can be taken to combat the arsenical vesicants other than treatment of the eyes which will be dealt with tomorrow are limited. The intense nasal irritation from ED may be combatted by inhalation of chlorine from bleach powder in a wide mouthed bottle. Respiratory pain may be relieved by steam inhalations of tincture of benzoin and menthol. Sulfonamide drugs should be administered as a preventive measure against bronchopneumonia.

Finally, to recapitulate, liquid burns of the eye may result in blindness, ulceration and perforation of the cornea. In the absence of the development of bronchopneumonia in respiratory cases not fatal within 48 hours, the prognosis is good. Arsenical poisoning is always to be feared from extensive liquid burns. In general most arsenical cases will be casualties for a shorter period of time than mustard cases in the absence of secondary infections and complications.



Physiological Class	Compound	Melting Point	Volatility in mg./l. at 20 C	Density of Saturated Vapor (air=1)	Persistence Summer	Persistence Winter	Minimum Detectable Conc. mg./l.	Intolerable Conc. mg./l. 1 min.	Lethal Conc. mg./l. 10 min.
Pul. irr.	MD	-42.5	74.4	5.5	1 hr.	2-3 hrs.	0.001 (irritation)	0.025	0.5
Vesicant								0.025	0.5
Lacrimator					1-2 hrs. open	2-4 hrs. open			
Sternutator	ED	-65	20	6.5	2-6 hrs. woods	12 hrs. woods	0.001 (irritation)	0.01	0.3
Systemic Poison									
	M-1	-18	4.5	7.1	24 hrs. open 1 wk. in woods	1 wk.	0.014 by odor 0.001 (irritation)	0.016	0.3
	PDA	-20	0.40	7.7	24 hrs. open 1 wk. in woods	more than 1 wk.	?		0.3

TABLE 1.

